Comparative evaluation of different doses of PPAR-γ agonist alone and in combination with sulfasalazine in experimentally induced inflammatory bowel disease in rats

Prasad Byrav D.S.¹, Bikash Medhi¹, Ajay Prakash¹, Amitava Chakrabarti¹, Kim Vaiphei², Krishan L. Khanduja

¹Department of Pharmacology, ²Department of Histopathology and ³Department of Biophysics, Postgraduate Institute of Medical Education and Research, Research Block B, Sector 12, PGMER, Chandigarh, India 160012

Correspondence: Bikash Medhi, e-mail: dbikash.5@yandex.com

Abstract:
Background: Inflammatory bowel disease (IBD) is an idiopathic, chronic inflammatory condition, which affects the gastrointestinal tract and has no curative treatment. The present study aimed to investigate the effect of different doses of pioglitazone alone and in combination with sulfasalazine in TNBS (trinitrobenzenesulfonic acid)-induced inflammatory bowel disease in rats.

Methods: A total of 36 animals were included in the study. Animals were divided into five groups (n = 6): group I – vehicle (ethanol), group II – TNBS + ethanol, group IIIA – TNBS + pioglitazone (15 mg/kg), group IIIB – TNBS + pioglitazone (30 mg/kg), group IV – TNBS + sulfasalazine (360 mg/kg), group V – TNBS + sulfasalazine (360 mg/kg) + pioglitazone (least effective dose found in group III). Group III was divided into two subgroups, namely IIIA and IIIB, on the basis of different doses of pioglitazone used. After completion of two weeks of treatment, rats were sacrificed under ether anesthesia by cervical dislocation for assessment of intestinal inflammation, histological analysis, myeloperoxidase assay, malondialdehyde assay and TNF-α estimation.

Results: All the drug-treated groups showed both gross morphological and microscopic score either 1 or 2. None of them showed score of > 2 on both gross and microscopic morphological examination. Both MDA levels and MPO activity were significantly reduced in the drug-treated groups, with maximum reduction seen in the combination group. TNF-α was reduced in pioglitazone group. It was highly reduced in sulfasalazine group (group V) as compared to TNBS group thereby indicating that pioglitazone is protective in TNBS-induced inflammatory bowel disease.

Conclusion: The present study showed reduction in lipid peroxidation, malondialdehyde levels and TNF-α levels in pioglitazone-treated group and hence, there was significant improvement in gross and microscopic features, too. However, combination of pioglitazone and sulfasalazine has shown greater efficacy.

Key words:
Inflammatory bowel disease, PPAR-γ, TNF-α, malondialdehyde, myeloperoxidase